UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/777,856	02/07/2001	Ami Aronheim	01/21605	3362

7590 02/08/2007

Martin D. Moynihan
PRTSI, Inc.
P. O. Box 16446
Arlington, VA 22215

EXAMINER	
MARVICH, MARIA	
ART UNIT	**PAPER NUMBER**
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/777,856	ARONHEIM ET AL.	
	Examiner	Art Unit	
	Maria B. Marvich, PhD	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 August 2006 and 17 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6-11,15-20,24-29,33-35,50 and 51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-11,15-20,24-29,33-35,50 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 June 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to a request for continued examination filed 7/20/06 and amendment filed 8/14/06 and 11/17/06. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/14/06 and 11/17/06 has been entered.

Claim Objections

Claims 1, 9, 18, 27 recite "detecting of restoration of said Ras signaling" in step (b) which encompasses conditions in which restoration would not be expected. It would be remedial to delete reference to "restoration of" and "said restoration of" and to recite -- detecting Ras signaling -- in section (b) such that conditions in which restoration is detecting and not detected are encompassed.

For accuracy, it would be remedial to recite -- each of said cells of said plurality of cells -- in claims 10, 19 and 28 rather then "each cell of said cells".

In claims 18 and 27, line 7, the claims recite that " said cells fused to a second polypeptide", whereas it appears it is the first polypeptide. It would be remedial to recite – wherein the first polypeptide is fused to a second polypeptide--.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 9-11, 15-20, 24-29, 33-35 and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **These are new rejections.**

Claims 9, 18 and 27 are vague and indefinite in that the metes and bounds of "a second polynucleotide of a library of polynucleotides" are unclear. This limitation recites that each cell from a plurality of cells comprises the same 2nd polynucleotide from a library is to be chosen. However, the claim also recites "each encoding a distinct prey polynucleotide fused to a cytoplasmic Ras mutant". As there is only one library, this phrase cannot be meant to identify each library. Therefore, it is unclear how to identify a 2nd polynucleotide from a library and also how this polynucleotide so recited can be distinct in each cell. It appears applicants are claiming a 2nd polynucleotide wherein this 2nd polynucleotide is from a library of polynucleotides and wherein each of these polynucleotides of the library encodes a distinct prey polypeptide fused to a cytoplasmic Ras mutant. If this is the case, it would be remedial to amend the language to state this. Similarly in claims 18 and 27, the claims recites "a first polynucleotide of a library of polynucleotides", which requires similar clarification.

Claim 18 is vague and indefinite in that the metes and bounds of "each operably linked to a first inducible promoter' are unclear. It is not clear to what "each" refers, the first polynucleotide or the library. It appears as if the claim intends that each of the polynucleotides of the library are operably linked to an inducible promoter. It would be remedial if this is the case

to recite, --wherein each of the polynucleotides of the library are operably linked to an inducible promoter--.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 6-11, 15-20, 24-29, 33-35, 50 and 51 are rejected under 35 U.S.C. 102(a) as being anticipated by Takemaru and Moon, The Journal of Cell Biology 149(2), April 17, 2000, pages 249-254, see entire document as evidenced by Ishakoff et al (EMBO, 1998, pages 5374-5387; see entire document) and Santangelo et al (ADH1 promoter). **The rejection of claims 1, 2, 6-8, 27-29 and 33-35 is maintained from the office action mailed 2/5/04 and 8/24/04 and 4/19/05 and 1/26/06. The rejection has been altered slightly based upon the amendment that both the first and second promoters are inducible. The rejection has thus been extended to claim 50. Upon reconsideration, claims 9-11, 15-20, 24-26 and 51 have been added to the rejection.**

Takemaru and Moon teach a method of identifying interactions between polypeptides comprising use of cdc25-2 yeast strain (endogenous ras is inactive and therefore the cell will lack Ras signaling). The cells were transfected with a first polynucleotide under control of an

inducible promoter encoding a polypeptide capable of interacting with a plasmalemma. This construct is cDNA fused to v-Src myristoylation sequences and under control of the galactose inducible promoter (page 250, col 2, paragraph 2 and page 251, col 1, paragraph 3). The cells were transfected with a second polynucleotide comprising a fusion of a second polynucleotide and a Ras cytoplasmic mutant. This vector is pRas(61)ΔF-βcatR8-C an expression vector comprising c-HaRas mutant fused to β-catenin (see e.g. page 251, column 1, paragraph 3). In a manner similar to the instant claims, the first construct is localized to the plasmalemma and as such functions as a bait for interacting prey peptides. Takemaru and Moon teach that pRas(61)ΔF-βcatR8-C is an expression vector comprising c-HaRas mutant fused to β-catenin inserted into 3SOB-SRS (Ishakoff et al, 1998). This vector as evidenced by Ishakoff et al expresses c-HaRas mutant fused to β-catenin under control of the ADH1 promoter (see e.g. page 5385, col 2, ¶ 2). The Adh1 promoter is an inducible promoter (see e.g. Santangelo). Cells were grown under inductive conditions, minimal galactose, and non-inductive conditions, minimal glucose. It is the difference between the two that indicates an interaction between a first and second polypeptide. Following growth of cells under inductive and non-inductive conditions, a clone expressing CBP in complex with b-catenin was identified upon isolation of a subset of cells (see e.g. page 251, column 1, paragraph 4) as in claim 28. The cdc25-2 cells are growth suppressive under non-permissive temperatures as in instant claim 6 and 33. This phenotype is corrected by translocation of the Ras mutant to the plasmalemma as in instant claim 7 and 34.

The v-Src myristoylation sequence is native to a v-Src gene and therefore meets the limitations of claim 2 and 28. Therefore, the library cDNAs fused to the v-Src myristoylation is on a vector that comprises an inducible galactose promoter driving expression of a first

polypeptide. The art has been applied as if this vector meets the limitation of claim 1 in that this is one polypeptide, which is a fusion between two polypeptide sequences and has been applied to meet the limitation of claim 27 in that v-Src is one polypeptide and the library cDNA encodes the second polypeptide. The art has been applied to meet the limitation that the Ras mutant is encoded by a second polynucleotide in that the broadest interpretation of a second polynucleotide of a library of polynucleotides is a single vector which absent evidence to the contrary could be isolated from other clonal variants.

Response to Arguments

Applicants traverse the claim rejections under 35 USC 102(a) on pages 10-12 of the amendment filed 8/14/06. Applicants' arguments filed 8/14/06 have been fully considered but they are not persuasive for the following reasons. It is applicants' arguments that the "bait" protein is a "known" protein and as such defines applicants "bait" protein as beta-catenin thus distinguishing Takemaru and Moon from the instant invention, which requires that the bait protein be a membrane protein. However, these distinctions are arbitrary. Rather there is nothing in claim 1 that limits the bait protein to one that is "known" while the "prey" protein is one that is unknown. As well, the functional role of the construct comprising cDNA fused to v-Src myristoylation sequences of Takemaru and Moon is the same as that of the instant claims, the first construct is localized to the plasmalemma and as such functions as a bait for interacting prey peptides. As such, anchored to the membrane, the peptide can be considered to function as bait. Secondly, Takemaru and moon do disclose use of a double inducible promoter as indicated

in the amended rejection above. As evidenced by Ishakoff et al and Santangelo, the vector used in the assay comprises an ADH1 promoter, which is an inducible promoter.

The Declaration filed on 8/14/06 under 37 CFR 1.131 has been considered but is ineffective to overcome the Takemaru and Moon reference. The Declaration does not provide requisite detail to demonstrate reduction to practice of the instant invention. The Declaration comprises correspondence with Nature discussing intention of submitting a paper to study protein-protein interaction specifically designed for membrane proteins. However, none of the details of the method are provided. While it is noted that the publication was published in Nature, the publication date antedates the reference in question and it is not possible to know what aspects of the invention were available at the time of the correspondence. Furthermore, the publication resulting from this correspondence has not been identified so it is not clear what aspects of the claimed invention were encompassed.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B. Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1633

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER